CLAIMS

We claim:

514/22
424/1.69

1. An isolated substantially homogeneous *mpl* ligand polypeptide.

530/391.1
435/6, 69.1
91.2
240.2
240.27
320.1
536/23.5

2. The *mpl* ligand polypeptide of Claim 1 selected from the group consisting of
   (a) a fragment polypeptide;
   (b) a variant polypeptide; and
   (c) a chimeric polypeptide.

3. The *mpl* ligand polypeptide of Claim 1 selected from the group consisting of
   (a) the polypeptide that is isolated from a mammal;
   (b) the polypeptide that is made by recombinant means; and
   (c) the polypeptide that is made by synthetic means.

4. The *mpl* ligand polypeptide of Claim 1 selected from the group consisting of
   (a) the polypeptide that is human; and
   (b) the polypeptide that is non-immunogenic in a human.

5. An isolated substantially homogeneous *mpl* agonist characterized in that:
   (a) the agonist stimulates the incorporation of labeled nucleotides (^{3}H-thymidine) into the DNA of IL-3 dependent Ba/F3 cells transfected with human *mpl* P; or
   (b) the agonist stimulates ^{35}S incorporation into circulating platelets in a platelet rebound assay.

6. An isolated *mpl* ligand polypeptide according to Claim 2, wherein the amino acid sequence of the polypeptide comprises amino acid residues 1 to X of **Fig. 8**, where X is selected from the group 153, 164, 191, 205, 207, 217, 229, 245 and 332.

7. The polypeptide of Claim 6 that is unglycosylated.

8. An isolated substantially homogeneous *mpl* ligand polypeptide sharing at least 80% sequence identity with the polypeptide of Claim 6.

9. An isolated polypeptide encoded by a nucleic acid having a sequence that hybridizes under moderately stringent conditions to the nucleic acid molecules having a nucleic acid sequence provided in **Fig. 8**.

10. The polypeptide of Claim 9 that is biologically active.

11. A chimera comprising the *mpl* ligand of Claim 6 fused to a heterologous polypeptide.

12. The chimera of Claim 2 consisting of the N-terminus 153 to about 157 hML residues substituted with one or more, but not all, of the human EPO residues added or substituted into the hML sequence at positions corresponding to the alignment shown in **Fig. 9**.

13. An antibody that is capable of binding the *mpl* ligand polypeptide of Claim 6.

14. A hybridoma cell line producing the antibody of Claim 13.

15. An isolated nucleic acid molecule encoding the *mpl* ligand polypeptide of Claim 1.

16. An isolated nucleic acid molecule encoding the *mpl* ligand polypeptide of Claim 6.

17. An isolated nucleic acid molecule comprising the open reading frame nucleic acid sequence shown in **Fig. 8** .

18. An isolated nucleic acid molecule selected from the group consisting of
(a) a cDNA clone comprising the nucleotide sequence of the coding region of the *mpl* ligand gene;
(b) a DNA sequence capable of hybridizing under stringent conditions to a clone of (a); and
(c) a genetic variant of any of the DNA sequences of (a) and (b) which encodes a polypeptide possessing a biological property of a naturally occurring *mpl* ligand polypeptide.

19. An isolated DNA molecule having a sequence capable of hybridizing to a DNA sequence provided in **Fig. 8** under moderately stringent conditions, wherein the DNA molecule encodes a biologically active *mpl* ligand polypeptide.

20. The nucleic acid molecule of Claim 15 further comprising a promoter operably linked to the nucleic acid molecule.

21. An expression vector comprising the nucleic acid sequence of Claim 15 operably linked to control sequences recognized by a host cell transformed with the vector.

22. A host cell transformed with the vector of Claim 21.

23. A method of using a nucleic acid molecule encoding the *mpl* ligand polypeptide to effect production of the *mpl* ligand polypeptide comprising culturing the host cell of Claim 22.

24. The method of Claim 23 wherein the *mpl* ligand polypeptide is recovered from the host cell.

25. The method of Claim 23 wherein the *mpl* ligand polypeptide is recovered from the host cell culture medium.

26. A method of determining the presence of *mpl* ligand polypeptide, comprising hybridizing DNA encoding the *mpl* ligand polypeptide to a test sample nucleic acid and determining the presence of *mpl* ligand polypeptide DNA.

27. A method of amplifying a nucleic acid test sample comprising priming a nucleic acid polymerase reaction with nucleic acid encoding a *mpl* ligand polypeptide.

28. A composition comprising the *mpl* ligand polypeptide of Claim 1 and a pharmaceutically acceptable carrier.

29. A method for treating a mammal having or at risk for thrombocytopenia comprising administering to a mammal in need of such treatment a therapeutically effective amount of the composition of Claim 28.

A 105 126

30. The composition of Claim 28 further comprising a therapeutically effective amount of an agent selected from the group consisting of a cytokine, colony stimulating factor, and interleukin.

31. The composition of Claim 30 wherein the agent is selected from LIF, G-CSF, GM-CSF, M-CSF, EPO, IL-1, IL-2, IL-3, IL-5, IL-6, IL-7, IL-8, IL-9 and IL-11.

Add B5